American Journal of Epidemiology
Vol. 155, No. 6
Printed in U.S.A.

Residential Radon and Lung Cancer Risk in a High-exposure Area of Gansu Province, China

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In the general population, evaluation of lung cancer risk from radon in houses is hampered by low levels of exposure and by dosimetric uncertainties due to residential mobility. To address these limitations, the authors conducted a case-control study in a predominantly rural area of China with low mobility and high radon levels. Included were all lung cancer cases diagnosed between January 1994 and April 1998, aged 30–75 years, and residing in two prefectures. Randomly selected, population-based controls were matched on age, sex, and prefecture. Radon detectors were placed in all houses occupied for 2 or more years during the 5–30 years prior to enrollment. Measurements covered 77% of the possible exposure time. Mean radon concentrations were 230.4 Bq/m^3 for cases (n = 768) and 222.2 Bq/m^3 for controls (n = 1,659). Lung cancer risk increased with increasing radon level ($p < 0.001$). When a linear model was used, the excess odds ratios at 100 Bq/m^3 were 0.19 (95% confidence interval: 0.05, 0.47) for all subjects and 0.31 (95% confidence interval: 0.10, 0.81) for subjects for whom coverage of the exposure interval was 100%. Adjusting for exposure uncertainties increased estimates by 50%. Results support increased lung cancer risks with indoor radon exposures that may equal or exceed extrapolations based on miner data. *Am J Epidemiol* 2002;155:554–64.

environment and public health; lung neoplasms; radiation; radon

Studies of underground miners demonstrate that exposure to radioactive radon gas and its decay products increases the risk of lung cancer (1). Although significant risks have been observed for miners exposed to low levels and receiving cumulative exposures comparable to those obtained by residing long term in houses with high levels of radon (2), direct demonstration of excess risks from residential radon is needed to confirm the risk of residential exposures and to affirm miner extrapolations.

Several case-control studies of residential radon have been conducted (3–14). Some studies have found no risk with indoor radon exposure, while others are consistent with increasing risk with increasing indoor exposure. Meta-analyses report a statistically significant excess risk from radon exposure (15, 16) but also indicate significant heterogeneity among studies, although such variability is expected (17, 18).

Low levels of exposure to residential radon, resulting in small excess risks, and uncertainties from reconstructing historic exposures have hampered evaluation of risk (3, 11, 19, 20). To address these limitations, we conducted a case-control study in an area of China where indoor radon concentrations are high and residential mobility is low.

MATERIALS AND METHODS

Study area

The study was conducted in Pingliang and Qingyang, rural prefectures in Gansu Province, China, with an adult population of about 4 million. Prior to 1976, most residents lived in underground dwellings; however, since 1976, many have moved to aboveground houses. In our study population, 99 percent had lived in an underground dwelling sometime during their lives.

Underground dwellings consist of several rooms, each a tunnel 5–10 m long, constructed around an excavated courtyard. There are four basic designs: underground cave dwellings, open-cut cave dwellings, ground cave dwellings, and aboveground cave dwellings. Aboveground cave dwellings are constructed on the surface and have thick walls, high ceilings, and other characteristics that mimic under-

Received for publication June 13, 2001, and accepted for publication September 18, 2001.

Abbreviations: CI, confidence interval; GSD, geometric standard deviation.

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ground types (21–23). People also live in standard aboveground dwellings with one or two stories, a single ridged roof and rectangular rooms, and multilevel apartments. A stove, which burns coal or other biomass, provides heating. The chimney is routed under a brick sleeping platform called a *kang*, then vented outside. Fuel is added to the firebox through an access door located either inside or outside the house.

Study subjects

Beginning in June 1995 and following approval by institutional review boards, we identified all persons aged 30–75 years who were diagnosed with lung cancer between January 1994 and April 1998 and lived in the two prefectures. Cases were ascertained from each prefecture hospital, a company hospital located at a nearby oilfield, 15 county hospitals, and local clinics. We also reviewed records from antituberculosis stations and from hospitals in the large nearby cities of Lanzhou, Xian, Baoji, and Yinchuan to identify lung cancers diagnosed in residents of the two prefectures.

On the basis of clinical/radiologic symptoms suggestive of lung cancer or pathologic evidence, 1,209 possible cases were identified. An expert panel of pathologists, radiologists, and clinicians from the Gansu Department of Health reviewed all diagnoses. The panel excluded 271 subjects because of insufficient supporting evidence or incorrect diagnosis, leaving 938 cases. Of those cases, 43 could not be located, 6 were outside the age range, and 3 had moved from the area; therefore, 886 cases remained (656 males, 230 females). Diagnoses of lung cancer were based on clinical/radiologic criteria for 533 cases (60 percent) and on pathologic evidence for 353 cases (40 percent). Among the clinically/radiologically identified cases, 414 (78 percent) died before the study period ended.

We randomly selected 1,968 controls from a list of all persons included in the 1990 population census and frequency matched on age in 1995 to cases in 5-year age groups, within categories of sex and prefecture. The number of controls in each stratum was based on twice the expected number of lung cancers derived from a 1991 medical records review. Among controls, 6 refused to be interviewed, 23 had moved from the area, 62 could not be located, 73 died before 1994, 4 became cases, and 35 were not interviewed for other reasons. The study enrolled 1,310 male and 455 female controls.

After informed consent was obtained, interviews were conducted at home or at the hospital by trained interviewers using a closed-form, structured questionnaire. We asked questions on demographic characteristics, smoking habits, diet and cooking practices, and occupational, residential, and medical histories. If a subject was deceased or was too ill to participate, the interview was conducted with his or her next of kin, usually the spouse. Surrogates provided information for 481 (54 percent) cases and 71 (4 percent) controls.

Radon measurements

Interviewers placed two 1-year alpha-track detectors in each respondent's house (Track-etch; TechOps-Landauer, Glenwood, Illinois), one in the living area and one in the sleeping area. Detectors were placed in all former houses in the study area that the subject occupied for 2 or more years during the previous 30 years. For quality assurance, we placed colocated detectors in 20 percent of the houses.

We conducted a substudy to investigate variation in radon levels within and between rooms, between dwellings, and over time to provide data to adjust for exposure variability. We placed six 1-year alpha-track detectors in each room (two each at the front, middle, and back) of 55 houses during 3 consecutive years, starting in July 1996. A total of 1,654 detectors were placed in one to five rooms of each house (mean, 2.3 rooms/house).

Assignment of radon exposure

We defined reference age as age at diagnosis for a case and at interview for a control. We designated 5–30 years prior to the reference age as the time-relevant exposure period most related to lung cancer risk (1). For nearly all cases (881 of 886) and controls (1,761 of 1,765), at least one radon measurement was available. For 88 percent (775 of 881) of cases and 95 percent (1,669 of 1,765) of controls, at least one measurement was within the exposure window from 1.9 (for cases) and 1.6 (for controls) mean eligible residences per subject.

For analysis, we used time-weighted average radon concentration within the exposure window measured in becquerels per cubic meter (Bq/m^3), using number of years resident as weights. (Becquerel is an international unit of radioactivity; 1 Bq = 1 disintegration per second.) Two controls had elevated radon values (1,554 and 1,676 Bq/m^3) that were more than 40 percent higher than the next-largest value and were omitted from our analyses, although this exclusion had little impact on inference. We imputed values for gaps in residential histories due to missing measurements or for less than 2 years of occupancy by using mean radon concentration in the houses of controls, within house type and prefecture (24). Alternatives, such as mean radon level within prefecture, made little difference. To adjust variances for imputation, we selectively computed estimates by using multiple imputation (25, 26), but variance correction proved unnecessary because of high coverage of the exposure window.

Statistical analysis

We computed odds ratios adjusted for age, sex, prefecture, tobacco use, and, where appropriate, other factors by using unconditional logistic regression (27). We calculated 95 percent Wald confidence intervals for odds ratios and used a score statistic for tests of trend. We also fitted a linear model, odds ratio(x) = $1 + \beta x$, in which x was the mean radon level and β was the excess odds ratio per becquerel/cubic meter. We computed likelihood-based confidence intervals for estimates of β. Homogeneity of β across categories of other factors was evaluated by using a likelihood ratio test.

Three important sources of error in assessing radon exposure were 1) detector measurement error, 2) use of contemporary measurements to estimate radon levels throughout the house and in prior years, and 3) missing radon values. Detector error was relatively small and was ignored. Estimation of radon induced classical error, while missing data induced Berkson error (3, 19). To adjust for error, we restricted data to subjects for whom coverage of the exposure window was 70 percent or higher, thus minimizing Berkson error, so that classical error predominated.

Specifically, suppose that X_i was the true, but unobserved radon concentration in the ith house within the exposure period, P_i was the proportion of years spent in the ith house, and Z_i was the estimated concentration. Further suppose that true radon exposure for a person was 25 times $\Sigma_i P_i X_i$, while observed radon exposure was 25 times $\Sigma_i P_i Z_i$. We assumed that each X_i was lognormally and independently distributed with parameters μ and σ^2 and that U_i was a multiplicative random error, independent of X_i and lognormally distributed with parameters 0 and τ^2. Then, $Z_i = X_i \times U_i$ and is lognormally distributed with parameters μ and $\sigma^2 + \tau^2$. Measurement data obtained from houses in the full study provided estimates of μ and $\sigma^2 + \tau^2$, while the radon substudy provided an estimate of τ^2.

For houses included in the substudy, arithmetic means were 366.5, 338.4, 378.1, 361.0, and 343.2 Bq/m^3 for underground cave dwellings, open-cut cave dwellings, ground cave dwellings, aboveground cave dwellings, and standard aboveground dwellings, respectively. The corresponding geometric means (and geometric standard deviations (GSDs)) were 338.7 Bq/m^3 (1.52), 314.2 Bq/m^3 (1.50), 347.6 Bq/m^3 (1.52), 336.0 Bq/m^3 (1.48), and 311.2 Bq/m^3 (1.58). Apartments were not included in the substudy. Houses had not been modified extensively, so we estimated τ^2 by assuming that uncertainties resulted from random variations in radon concentration within houses and over time and that residential mobility was unrelated to radon, conditional on housing type. Use of a component of variance analysis estimated τ^2 as 0.16, or a GSD of about 1.5 for the error distribution. We evaluated a range of GSDs—1.25, 1.5, and 1.6 (or coefficients of variation of 0.23, 0.42, and 0.50)—to investigate the sensitivity of the error on the excess odds ratio.

Under our assumptions, the true value given the observed value, denoted $X_i|Z_i$, was lognormally distributed with parameters $(\mu\, \tau^2 + \log(Z_i)\, \sigma^2)/(\tau^2 + \sigma^2)$ and $\tau^2\, \sigma^2/(\tau^2 + \sigma^2)$ (18). We used a Monte Carlo approach to evaluate error. For each subject's house, we randomly sampled from the $X_i|Z_i$ distribution, computed a "true" time-weighted average radon concentration, and estimated the excess odds ratio per becquerel/cubic meter. This process was repeated 1,000 times to obtain the empirical distribution of the estimated β and its 95 percent confidence interval. This approach was less formal than the one used by Reeves et al. (19) but was similar to the Lagarde et al. approach (20).

RESULTS

Demographic and other risk factors

There were 768 cases (563 males and 205 females) and 1,659 controls (1,232 males and 427 females) for whom radon measurements and data on the primary adjustment factors were available. Although matching criteria included age, controls were older than cases (table 1). Controls were selected from a list of all persons included in the 1990 population census on the basis of their age in 1995. Ages were slightly higher than anticipated because controls were generally interviewed after cases and enrollment was extended for 6 additional months.

Cases had more education, higher incomes, and fewer cattle, and they were more likely to own a color television and a refrigerator. We adjusted for ownership of a color television and for number of cattle, both representing socioeconomic factors, and for age, sex, and prefecture.

Most men smoked (92.3 percent), but most women did not (10.4 percent). The odds ratio for ever smokers compared with never smokers was 1.69 (95 percent confidence interval (CI): 1.2, 2.4) and was similar for males and females. Empirical analyses indicated that the increase in the logarithm of the odds ratio per manufactured cigarette smoked per day was one third the increase per *liang* (50 g) of tobacco smoked per month in hand-rolled cigarettes and about the same per *liang* of tobacco smoked per month in a pipe. We used these results to create cigarette-equivalents per day by summing number of cigarettes smoked per day, 3.0 times *liang* per month smoked in hand-rolled cigarettes, and *liang* per month smoked in pipes. Among smokers, cases and controls smoked 17.9 and 12.9 cigarette-equivalents per day for 30.3 and 29.7 years, respectively. We also created a smoking risk variable to account for duration and number of cigarette-equivalents smoked per day (table 2). Odds ratios increased with increasing tobacco exposure and were homogeneous by sex.

Radon measurements

Radon detector values for 3,188 houses measured are displayed in figure 1, panel A. The arithmetic mean was 222.9 Bq/m^3, the geometric mean was 176.2 Bq/m^3, and the GSD was 2.08. Radon levels varied according to the style of the house; arithmetic means were 306.0, 299.4, 238.7, 274.9, 207.2, and 69.0 Bq/m^3 for underground cave dwellings, open-cut cave dwellings, ground cave dwellings, aboveground cave dwellings, standard aboveground dwellings, and apartments, respectively. Detector measurements exhibited less skewness compared with the estimated lognormal distribution (figure 1, panel A). This pattern was similar when houses were classified by indoor smokiness, type of fuel used (coal, firewood, and sticks and twigs), and housing type (not shown).

We hypothesized that ventilation reduced radon levels while increasing variability. Figure 1 shows that concentrations of less than (panel B) and more than (panel C) 150 Bq/m^3 were consistent with a lognormal distribution, with greater variability at lower concentrations. For comparison with panel A, arithmetic means and geometric means in panels B and C show values for the unconditional lognormal distributions.

Radon exposure

Mean radon concentrations for cases and controls were 230.4 and 222.2 Bq/m^3, respectively, and those for 81.6 per-

TABLE 1. Distribution of subjects and odds ratios* for lung cancer by categories of demographic variables, Gansu Province, China, 1994–1998

Variable	Males			Females		
	Cases (%)	Controls (%)	OR	Cases (%)	Controls (%)	OR
Reference age (years)						
<45	13.3	11.5	1.00†	17.1	11.5	1.00†
45–54	28.8	30.0	0.80	36.5	36.8	0.69
55–64	40.7	34.3	0.99	32.2	32.6	0.69
≥65	17.2	24.2	0.61‡	14.2	19.2	0.55
Prefecture						
Pingliang	51.0	44.3	1.00†	47.8	56.2	1.00†
Qingyang	49.0	55.7	0.77‡	52.2	43.8	1.34
Education						
Primary or less	68.4	80.1	1.00†	88.8	95.8	1.00†
Technical/vocational	28.9	18.8	1.80	10.8	3.7	2.78
College or more	2.7	1.1	2.79‡	0.5	0.5	1.17‡
Marital status						
Married	90.9	89.0	1.00†	86.8	85.2	1.00†
Widowed	8.2	9.1	0.99	12.7	14.8	0.99
Divorced	0.4	1.1	0.31	0.5	0.0	
Never married	0.5	0.8	0.65	0.0	0.0	
Income (renminbi§)						
<2,000	23.9	24.0	1.00†	22.0	25.0	1.00†
2,000–2,999	18.0	24.1	0.74	16.6	19.8	0.99
3,000–4,799	28.9	31.0	0.94	26.8	28.3	1.16
≥4,800	29.1	20.9	1.40‡	34.6	26.9	1.54‡
No. of persons in household						
1–2	6.4	6.9	1.00†	9.3	5.6	1.00†
3–4	29.7	26.4	1.13	23.5	23.7	0.53
5–6	40.4	44.1	0.94	43.6	42.7	0.57
≥7	23.4	22.6	1.06	23.5	27.9	0.50
Own¶						
Television						
Black and white	49.5	50.1	0.96	46.1	50.6	0.83
Color	33.4	19.0	2.14‡	31.3	17.3	2.31‡
Tape recorder	36.3	34.4	1.05	29.8	27.4	1.13
Refrigerator	6.4	1.8	3.88‡	6.4	2.1	3.15
No. of cattle						
0	48.3	30.2	1.00†	52.7	33.3	1.00†
1	29.0	30.9	0.56	22.4	33.5	0.42
≥2	22.7	38.0	0.35‡	24.9	34.2	0.45‡
No. of vehicles (≥1)	7.3	7.4	0.97	9.3	6.8	1.42
Total no.#	563	1,232		205	427	

* Odds ratios (ORs) were adjusted for age and prefecture.
† Referent category.
‡ Test of trend of odds ratios, $p < 0.01$.
§ 1 renminbi = US $0.12.
¶ Referent category, nonownership of item.
# Numbers differ for each variable because of missing data.

cent of cases and 76.3 percent of controls were at or above 150 Bq/m^3. Odds ratios increased significantly with increasing concentration ($p < 0.001$) (table 3, figure 2). The test for departure from linearity was not significant ($p = 0.10$). The estimated excess odds ratio at 100 Bq/m^3 was 0.19 (95 percent CI: 0.05, 0.47).

Coverage of the exposure window ranged from 8 to 100 percent, with a mean of 76.7 percent (71.6 percent for cases and 79.1 percent for controls). We restricted data by coverage, assuming that greater coverage indicated improved exposure assessment and thus reduced misclassification. Among subjects for whom coverage was 70 per-

TABLE 2. Distribution of subjects, odds ratios,* and 95% confidence intervals by categories of smoking risk, Gansu Province, China, 1994–1998

Smoking category†	Males (%)		Females (%)		Cigarettes only		Pipes only		Mixed smokers‡		Total§	
	Cases	Controls	Cases	Controls	OR	95% CI¶	OR	95% CI	OR	95% CI	OR	95% CI
Never smoked	5.0	8.9	88.3	90.2	1.00		1.00		1.00		1.00	
Other smokers	53.3	60.3	10.2	8.4	1.28	0.8, 1.8	1.14	0.7, 1.8	2.61	1.7, 3.9	1.47	1.0, 2.1
Smoked ≥10 cigarettes/day ≥30 years	33.2	26.9	1.5	1.4	2.46	1.5, 4.1	1.69	1.0, 2.8	3.28	2.1, 5.1	2.38	1.6, 3.5
Smoked ≥20 cigarettes/day ≥40 years	8.5	3.9	0.0	0.0	5.47	2.2, 12.2	3.38	1.1, 10.7	3.98	1.9, 8.2	4.26	2.4, 7.4
Total no.	563	1,232	205	427								

* All odds ratios (ORs) were adjusted for reference age, sex, prefecture, and socioeconomic factors, as represented by ownership of a color television and number of cattle.

† Smokers were assigned to their most heavily exposed category. Duration denotes total years of smoking cigarettes and/or pipes, and amount denotes the sum of the number of cigarettes smoked per day and three times liang (1 liang = 50 g) smoked per month in hand-rolled cigarettes and liang per month smoked in pipes. "Other smokers" were light smokers not satisfying the criteria for the smoking categories.

‡ Includes cigarette and pipe smokers.

§ Odds ratios by smoking category did not vary significantly across smoking status (cigarettes only, pipes only, or mixed smokers), $p = 0.17$.

¶ CI, confidence interval.

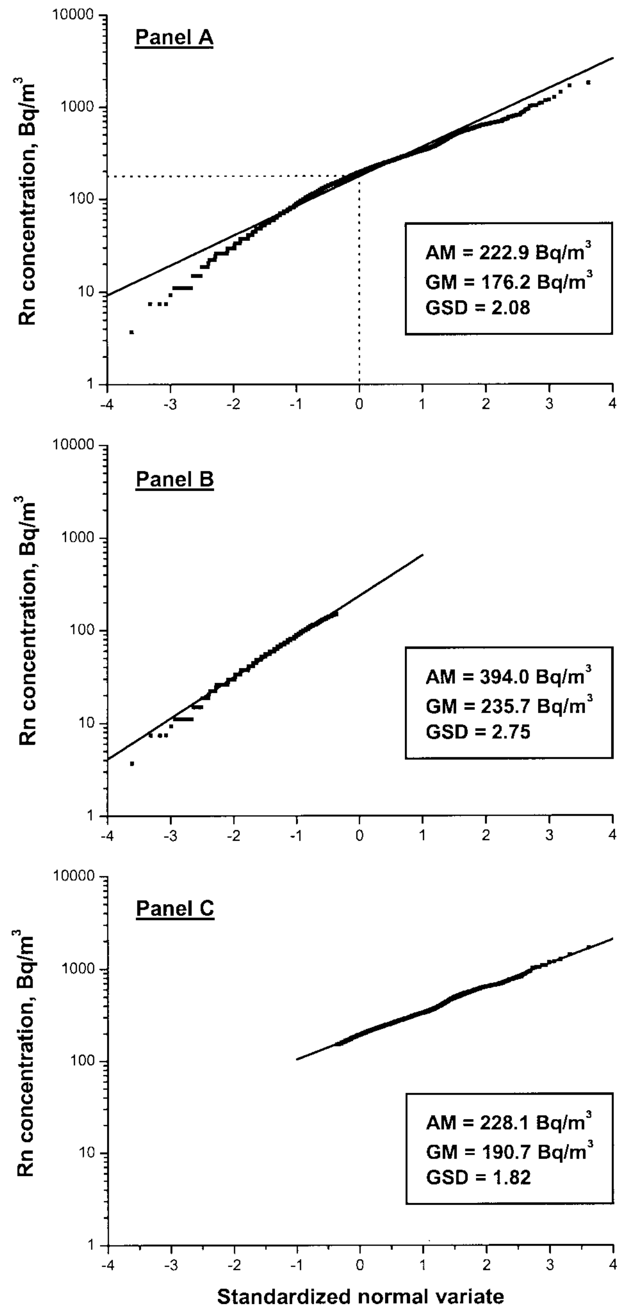

FIGURE 1. Probability plot, arithmetic mean (AM), geometric mean (GM), and geometric standard deviation (GSD) for all radon detector values (panel A) and for radon values less than or equal to (panel B) or greater than (panel C) 150 Bq/m^3 for the indoor radon study conducted in Gansu Province, China, 1994–1998. Estimates of AM, GM, and GSD for panels B and C reflect unconditional log-normal distributions.

cent or higher (463 cases and 1,143 controls with 98.1 percent coverage), 90 percent or higher (398 cases and 1,069 controls with 99.8 percent coverage), or 100 percent (366 cases and 1,045 controls) at 100 Bq/m^3, the excess odds ratios were 0.22 (95 percent CI: 0.06, 0.54), 0.26 (95 per-

TABLE 3. Odds ratios* for lung cancer, by time-weighted average radon concentration, for exposures 5–30 years prior to the referent age, Gansu Province, China, 1994–1998

Radon concentration (Bq/m^3)	No. of cases	No. of controls	Total no.	Mean concentration	OR†	95% CI‡
<100	61	166	227	69.3	1.00	
100–149	80	227	307	128.0	1.00	0.7, 1.5
150–199	190	355	545	178.0	1.42	1.0, 2.0
200–249	223	444	667	223.2	1.36	1.0, 1.9
250–299	83	198	281	273.6	1.28	0.8, 1.9
≥300	131	269	400	419.4	1.58	1.1, 2.3
Total	768	1,659	2,427	224.8§		

* Odds ratios (ORs) were adjusted for referent age, sex, prefecture, smoking risk, and socioeconomic factors, as represented by ownership of a color television and number of cattle.

† Excess odds ratio per 100 Bq/m^3 was 0.19 (95% confidence interval: 0.05, 0.47) based on the model OR(x) = 1 + βx, where x is the radon concentration.

‡ CI, confidence interval.

§ Mean radon concentrations for cases and controls were 230.4 and 222.2 Bq/m^3, respectively.

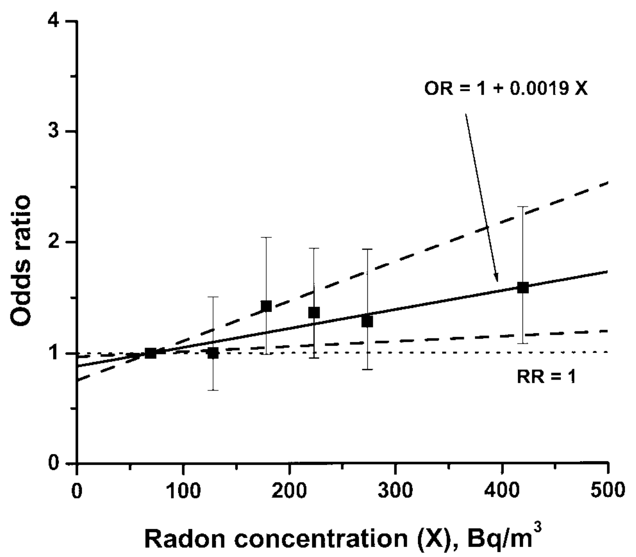

FIGURE 2. Odds ratios (OR) for categories of radon concentration located at means within category and the fitted linear excess odds ratio model (solid line), with 95% confidence limits (dashed lines), for the indoor radon study conducted in Gansu Province, China, 1994–1998.

cent CI: 0.08, 0.66), and 0.31 (95 percent CI: 0.10, 0.81), respectively.

There were 297 histologically confirmed cases of lung cancer. The excess odds ratios for an exposure level of 100 Bq/m^3 were 0.14 (95 percent CI: –0.03, 0.54) when confirmed cases were used and 0.20 (95 percent CI: 0.03, 0.55) when clinically diagnosed cases were used. Neither excess odds ratio differed significantly from the overall value of 0.19.

Table 4 shows the odds ratios for radon within categories of various other factors. There was no significant variation in radon effects by any factor except type of house. In addition, we found a suggestion of declining effects with reference age. Type of house, smokiness, and coal referred to the house in which a subject lived the longest, but results were similar for the current house. Heterogeneity was found in the excess odds ratio by type of house, with no trend for subjects living in standard aboveground dwellings or apartments. This difference in trend by house type was reduced when smoking and housing type were included as stratification variables and data were restricted. The excess odds ratios at 100 Bq/m^3 (and p values for homogeneity) for underground and standard housing types were 0.33 and 0.03 (p = 0.15), 0.32 and 0.10 (p = 0.35), and 0.35 and 0.17 (p = 0.54) when coverage of the exposure window was 70 percent or higher, 90 percent or higher, and 100 percent, respectively.

Next of kin were interviewed for 54.2 percent of the cases and 4.0 percent of the controls. When data were limited to subject respondents, the excess odds ratio estimate at 100 Bq/m^3 was 0.24 (95 percent CI: 0.03, 0.80), similar to the overall excess odds ratio estimate of 0.19.

Adjustment for uncertainty about radon exposure

Among subjects for whom coverage of the exposure window was 70 percent or higher, the excess odds ratios at 100 Bq/m^3, adjusted for error GSDs of 1.25, 1.5, and 1.6, were 0.27 (95 percent CI: 0.03, 0.69), 0.32 (95 percent CI: 0.08, 1.37), and 0.59 (95 percent CI: 0.14, 2.73), respectively, in contrast to the unadjusted estimate of 0.22 (95 percent CI: 0.06, 0.54). Excess odds ratio estimates, as well as the widths of the confidence intervals, increased with greater exposure error.

DISCUSSION

This large case-control study of lung cancer was carried out in an area of low residential mobility and high radon concentration. Mean radon concentration among the controls in our study was similar to that found in a study in Finland (9); about twice the mean concentration of radon in the Sweden national (7), Winnipeg, Canada (5), and Shenyang, China (14) studies; and about five times the US national mean (28). The overall excess odds ratio at 100 Bq/m^3 was 0.19 (95 percent CI: 0.05, 0.47). Adjustment for

TABLE 4. Odds ratios* for lung cancer by time-weighted radon concentration, Gansu Province, China, 1994–1998

Variable	No. of cases	No. of controls	OR for radon concentration (Bq/m³) <150	150–199	200–249	≥250	Excess OR at 100 Bq/m³†	*p* value‡
Reference age (years)								
<45	110	191	1.00	1.17	0.75	1.40	0.68	0.51
45–54	236	526	1.00	1.11	1.09	1.34	0.20	
55–64	295	562	1.00	1.92	2.24	1.81	0.22	
≥65	127	380	1.00	1.35	1.02	1.08	0.04	
Sex								
Male	563	1,232	1.00	1.28	1.41	1.35	0.22	0.62
Female	205	427	1.00	1.86	1.24	1.81	0.12	
Smoking status§								
Never smoked	209	495	1.00	2.09	1.19	1.62	0.09	0.39
I	338	793	1.00	1.19	1.17	1.45	0.34	
II	177	329	1.00	1.27	2.44	1.18	0.02	
II	44	42	1.00	0.95	0.61	2.71	0.80	
Previous diagnosis of pulmonary tuberculosis¶								
No	723	1,608	1.00	1.46	1.34	1.48	0.20	0.74
Yes	45	51	1.00	0.79	2.01	1.14	0.45	
Previous diagnosis of bronchitis or emphysema¶								
No	654	1,485	1.00	1.46	1.26	1.43	0.20	0.92
Yes	114	174	1.00	1.18	2.15	1.69	0.23	
Type of house								
Underground#,**	439	1,030	1.00	1.66	1.86	2.03	0.50	0.02
Standard	329	629	1.00	1.29	1.00	0.93	−0.01	
Smokiness of indoor air during winter cooking**								
Smoky	353	781	1.00	1.48	1.46	1.56	0.22	0.97
Not smoky	392	860	1.00	1.42	1.32	1.42	0.22	
Amount of coal used (kg)/year**								
None	344	924	1.00	1.33	1.46	1.88	0.26	0.21
<1,000	152	317	1.00	1.99	2.08	1.72	0.21	
≥1,000	248	401	1.00	1.29	1.16	0.90	0.09	

* Odds ratios (ORs) were adjusted for reference age, sex, prefecture, smoking risk, and socioeconomic factors, as represented by ownership of a color television and number of cattle.

† Excess odds ratio per 100 Bq/m³ based on the model $OR(x) = 1 + \beta x$, where x is the radon concentration.

‡ Test of homogeneity of the estimated excess odds ratios.

§ Smoking risk levels: I, other; II, duration ≥30 years and amount ≥10: cigarettes/day; III, duration ≥40 years and amount ≥20 cigarettes/day, with subjects classified in the highest risk category.

¶ Disease diagnosis by a physician ≥5 years prior to the referent age to minimize the possibility of differential bias.

\# Underground dwelling includes all cavelike housing styles. Standard dwelling includes the standard aboveground style and apartments.

** Refers to the house in which the subject lived the longest.

our best estimate of exposure uncertainty increased the excess odds ratio at 100 Bq/m^3 by about 50 percent.

There have been several case-control studies of residential radon and lung cancer in which long-term detectors were used (3–14). Meta-analyses of those studies estimated an excess odds ratio of 0.1–0.2 at 100 Bq/m^3 (3, 15, 16). Extrapolations based on results from miners exposed to low radon concentrations result in excess odds ratios of about 0.12 (2), similar to the combined estimate and slightly lower than the unadjusted estimate in our study.

Risk estimates from meta-analyses of residential studies and from pooled miner analyses do not account for errors in exposure assessment. Stability of our population may indicate improved exposure assessment, resulting in the higher excess odds ratio estimates. At 100 Bq/m^3, estimates of excess odds ratios were 0.22, 0.26, and 0.31 when data were limited to subjects for whom coverage of the exposure window was 70 percent or higher, 90 percent or higher, and 100 percent, respectively.

Three recent studies with enhanced exposure assessments also suggest that the risk of lung cancer may be higher than previously estimated. A study of Missouri women based exposure on CR-39 surface measurement devices and reported an excess odds ratio of 0.63 (95 percent CI: 0.1, 1.9) at 100 Bq/m^3 (11). These devices measure emissions from polonium-210 embedded in glass artifacts, such as picture frames and mirrors, which may better reflect historical exposure than contemporary air measurements, since the artifact serves as a continuous recording device. An Iowa study enrolled only long-term (20 years or more) residents, thereby minimizing uncertainties resulting from residential mobility (12). The exposure assessment included measurements throughout each house, residential occupancy, and time spent in other buildings and outdoors (29). The estimated excess odds ratios at 100 Bq/m^3 ranged from 0.16 (95 percent CI: 0.0, 0.6) for all subjects to 0.33 (95 percent CI: 0.02, 1.23) for living subjects. A study in Finland enrolled residents of 20 years or more and estimated the excess odds ratio at 100 Bq/m^3 as 0.11 (95 percent CI: 0.9, 1.3) (4).

Precise characterization of exposure error and adjustment of risk estimates are problematic. Previous adjustments increased excess odds ratio estimates by about 50–100 percent. In a southwest England study, the estimate of the excess odds ratio at 100 Bq/m^3 increased after adjustment from 0.08 (95 percent CI: –0.03, 0.20) to 0.12 (95 percent CI: –0.05, 0.33) for all subjects and from 0.14 (95 percent CI: 0.01, 0.29) to 0.24 (95 percent CI: –0.01, 0.56) for subjects among whom coverage of the exposure window was complete (3). Depending on error assumptions, excess odds ratio estimates in a Swedish study increased from 0.10 to 0.15–0.20 (20). Our best estimate of uncertainty increased the excess odds ratio by about 50 percent.

Our evaluation of exposure misclassification did not account for time spent in the house. Subjects reported spending about half their time indoors during adulthood. For males and females, mean occupancy during their adult years was 11.8 (49 percent) and 11.9 (50 percent) hours per day during summer months and 12.8 (53 percent) and 13.7 (57 percent) hours per day during winter months, respectively. Because most subjects were farmers, time not spent in their houses was likely spent outdoors. For our subjects, the length of occupancy was less than the assumed 60–90 percent found in North American and European studies (30). In our data, occupancy was related to reference age, increasing 1–1.5 hours between ages 40 and 70 years. However, we had no data on the variation in occupancy throughout life, which changes substantially during adulthood (12).

To our knowledge, there has been only one other large study of radon and lung cancer in China (14). That study, carried out in the northern industrial city of Shenyang, included 308 lung cancer cases and 356 controls. Odds ratios for all radon categories were less than one and were nonsignificant. The absence of significant findings may reflect the urban location, the higher levels of outdoor air pollution, or lower radon levels, which were measured in only a single house per subject. Subjects reported a median of 24 years of residency, which represents 19 years in the 5–30-year exposure-relevant period, and a median radon level of 85 Bq/m^3, about 60 percent lower than in our study. For subjects in our study who had occupied their current house for at least 5 years, mean coverage was 28 of the previous 30 years, which represents 23 years during the exposure-relevant period.

Analyses of miners have suggested that the relative risk trend for radon is higher for never smokers and younger persons (1). Indoor radon studies, including the current one, show inconsistent patterns of risk by smoking status and age (table 5). Excess odds ratios seemed to decline with increasing attained age in the Finland-II (4), Missouri-I (8), Missouri-II (11), southwest England (3), and Stockholm, Sweden (6) studies and suggestively in our study, but they did not vary in the Finland-I (9) and Iowa (12) studies. Data from the Stockholm study and living respondents in the Missouri-I study provide only suggestive evidence for a greater odds ratio trend with radon exposure for never smokers.

Reasons for the differences in risk patterns for miners and residentially exposed subjects are unclear. Comparative dosimetry suggests an approximate equivalence between dose to target tissue for a given exposure in mines and in houses (31). However, dosimetry comparisons do not take into account other differences in the two environments, such as exposure to other lung carcinogens and lung irritants in mines. Another possible reason for the differences is low power in individual studies to evaluate subtle variations, since residential risks are small and exposures are estimated with uncertainty (18).

Because miner studies included males only, these studies are uninformative about radon risks for females. Risk extrapolations to females for residential exposures have relied on the assumption of equivalent susceptibility (1). There is evidence from the Finland-II (4) and southwest England (3) studies that the excess odds ratio for radon is higher for males than for females; however, our study suggests no such difference (table 5). The question of differential effects by sex remains unresolved.

A potential confounder in our study was indoor air pollution, since most subjects used coal, wood, or sticks in a stove or *kang* for cooking and heating. In April 1995, we measured particle-bound polycyclic aromatic hydrocarbons, particulate matter smaller than 10 microns (PM_{10}), carbon monoxide, nitrogen dioxide, sulfur dioxide, and air exchange rate in 25 dwellings (22, 32). Ventilation rates were high, averaging 1.5 air exchanges per hour, and resulted in pollutant levels that were episodic and elevated only during stove use. Except for carbon monoxide and PM_{10}, mean values were below US Ambient Air Quality Standards (for more information, refer to the following Internet Web site: http://www.epa.gov/airs/criteria.html). We did not have air pollutant measurements for each study house; however, odds ratios for radon did not vary significantly with level of indoor smokiness as reported by the respondent. Odds ratio trends for radon were similar by house type after we included smoking risk and house type as stratification variables.

Information on more than half of our cases came from their next of kin, who may have been less knowledgeable about life events, raising the possibility that results might have been affected by differential misclassification. However, odds ratios were similar after adjustment for source of information or when data were restricted to subject respondents only.

TABLE 5. Summary of excess odds ratios at a radon concentration of 100 Bq/m³ and 95% confidence intervals overall and within categories of effect modification factors in published residential radon studies, with *p* values for results of tests of homogeneity of excess odds ratios across categories

Study (cases/controls) (reference no.)	Overall excess OR* (95% CI*)	Sex	Age at diagnosis (years)	Smoking	Other
Current study M: 563/1,232 F: 205/427	All subjects: 0.19 (0.05, 0.47)	M*: 0.22 F*: 0.12 *p* = 0.62	<45: 0.68 45–54: 0.20 55–64: 0.22 ≥65: 0.04 *p* = 0.51	Never: 0.09 I†: 0.34 II: 0.02 III: 0.80 *p* = 0.39	Refer to table 4
Finland-I‡ (9) M: 164/331	0.57 (0.27, 0.99)		<55: −0.29 55–64: 0.0 ≥65: 0.81 *p* = 0.67	Former: 0.10 1–9§ 10–20: 0.38 ≥20: −0.19 *p* = 0.99	
Finland-II (4) M: 479/479 F: 38/38	0.11 (−0.06, 0.31)	M: 0.16 F: −0.45 *p* = 0.04	≤60: 0.19 61–69: 0.14 ≥70: 0.02 *p* = 0.83	Never: −0.28 Former: 0.23 1–9§: 0.20 10–19: −0.13 ≥20: 0.35 *p* = 1.00	Occupational asbestos: Never: 0.21 Ever: −0.23 *p* = 0.03
Iowa (12) F: 413/614	All subjects: 0.16 (−0.03, 0.61) Living subjects: 0.33 (0.02, 1.23)		40–59: 0.12 60–69: 0.13 70–84: 0.21 *p* = 0.93	Never: 0.15 Light¶ 0.22 Heavy: 0.09 *p* = 0.83	Education (no. of years) <12: −0.05 12: 0.14 ≥12: 0.23 *p* = 0.71
Missouri-I# (8) F: 538/1,183	All subjects: 0.05 (−0.13, 0.24) Living subjects: 0.47 (0.03, 1.40)		All: Living: <65: 0.61 0.89 65–74: 0.03 0.40 ≥75: 0.08 0.27 *p* = 0.11 0.77	All: Living: Never: 0.06 0.73 Former: 0.02 0.08 *p* = 0.89 0.28	
Missouri-II (11) F: 372/471 (surface) 247/299 (air)	Surface monitors: 0.63 (0.07, 1.93) Air monitors: 0.04 (−0.13, 0.57)		Surface: Air: <65: 0.80 0.06 65–74: 0.47 −0.17 ≥75: 0.53 1.93 *p* = 0.84 0.13	Surface: Air: Never: 0.20 −0.22 Former: 0.27 0.18 Light to medium: 0.73 −0.32 Heavy: 2.53 1.08 *p* = 0.84 0.08	Education**: <12, 1.07 12, 0.6 ≥13, 0.4 *p* = 0.05 Previous lung disease: No, 2.27 Yes, 0.97 *p* = 0.05 Vegetable servings/week: <7, 0.4 7, 2.2 ≥8, 0.47 *p* = 0.05

New Jersey‡ (10) F: 433/402	0.28 (−0.28, 0.97)			Never: 0.03 <15:‡ 3.18 15–24: 1.17 ≥25: −0.43 *p* = 0.43	
Shenyang, China‡ (14) F: 308/356	−0.04 (−0.23, 0.19)			Never: −0.13 Light††: −0.16 Heavy: 0.10 *p* = 0.58	
Southwest England (3) M: 667/2,108 F: 315/1,077	All subjects: 0.08 (−0.03, 0.20) Complete 30-year 0.14 (0.01, 0.29)	M: 0.14 F: −0.18 *p* = 0.05	<55: 0.31 55–64: −0.06 65–76: 0.10 *p* = 0.36	Never: 0.04 Current: −0.04 Former: 0.19 Other: −0.23 *p* = 0.42	No. of years worked outdoors: 0: −0.03 1–20: 0.12 ≥21: 0.22 *p* = 0.36
Stockholm, Sweden‡ (6) F: 210/310	0.52 (−0.05, 1.54)		<55: 0.99 55–64: 0.31 ≥65: 0.07 *p* = 0.58	Never: 1.01 Former: 0.08 1–9§: 0.50 ≥10: 0.38 *p* = 0.52	
Sweden (7) M: 774/1,467 F: 586/1,380	0.10 (0.01, 0.22)			Never: 0.07 Former: 0.01 1–9§: 0.16 ≥10: 0.19 *p* = 0.68	
Winnipeg, Canada (5) M: 488/488 F: 250/250	−0.06 (−0.14, 0.05)				
Western Germany (13) M: 1,214/1,865 F: 235/432	All subjects: −0.02 (−0.18, 0.17) Radon-prone areas: 0.13 (−0.12, 0.46)				

* OR, odds ratio; CI, confidence interval; M, male; F, female.
† Smoking categories: I, other; II, duration ≥30 years and amount ≥10 cigarettes/day; III, duration ≥40 years and amount ≥20 cigarettes/day, with subjects classified in the highest risk category.
‡ Estimates and tests from weighted regression, with reciprocals of the sums of the inverse numbers of cases and of controls as weights, using a linear odds ratio model.
§ No. of cigarettes smoked per day.
¶ Smoking categories: light, smoked <208.2 packs/year; heavy, smoked >208.2 packs/year.
# Based on linear model for odds ratio applied to original data.
** Results for surface detectors placed on glass artifacts.
†† Smoking categories: light, smoked for <30 years or smoked 1–19 cigarettes/day for <40 years; heavy, smoked ≥20 cigarettes for ≥30 years or smoked for ≥40 years.

In conclusion, radon concentrations were high in our study, exceeding those found in most previous indoor studies, and the population was stable and rural. Results provide evidence that high levels of residential radon increase the risk of lung cancer and support the findings from meta-analyses of indoor studies and from miners. In addition, our estimates suggest that effects of residential radon may equal or exceed miner-based estimates, which are currently used to evaluate risk.

ACKNOWLEDGMENTS

This work was partially supported by Interagency Agreement Y01-CP5-0260 between the US Environmental Protection Agency and the National Cancer Institute.

The authors acknowledge the contributions of Drs. Jiguo Shi, Yuelan Kang, Datong Zhao, Fuhui Du, and Yucheng Wang for identifying lung cancer cases, and they thank the many local investigators from Pingliang and Qingyang Prefectures for their assistance with data collection. The authors also thank all those persons who contributed to part of the project as well as Margaret Pacious and Lew Gaul of WESTAT, Inc. for program management and data processing support for this study.

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